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CENTRAL INTELLIGENCE AGENCY

# INFORMATION REPORT

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COUNTRY East Germany

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SUBJECT Production of Digitoxin at Arzneimittelwerk Dresden

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THIS IS UNEVALUATED INFORMATION

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1. During the course of preparation of "Panlanat" [1] at Arzneimittelwerk-Dresden (AWD), an attempt was made to prepare pure digitoxin. The research laboratory of the AWD was successful in producing about 15 grams of this product in 1953. There was considerable difficulty in the preparation of the digitoxin because of a misunderstanding of the descriptions of "pure" digitoxin available in Dresden. The definition of digitoxin in USP XIV stated that the glycoside mixture and the gitoxin fraction should correspond to official requirements. One author (McChesney) found 10.6 percent gitoxin in one preparation analyzed. Furthermore, the recommended purity varied in different drug tests. The USP XIV stated that digitoxin, or a mixture of heart-active glycosides from Digitalis purpurea, was pure when it consisted essentially of digitoxin and gitoxin.

2. In March 1953, the following procedure was used to produce digitoxin:

   a. The first part of the procedure was carried out at the former Madaus plant [2] on Gartenstrasse 19. Fifty kilograms of folia Digitalis purpurea were macerated in cold water and allowed to stand for 24 hours. After filtration the drug was again treated with cold water for the same length of time and refiltered. The aqueous extract was discarded and the residue extracted three times, each for two-day periods, with 45 percent methanol. A total of 500 kilograms of methanol were used. The combined extracts weighed 470 kilograms.

   b. The methanol extract was precipitated by adding six liters of 10 percent lead acetate solution. During the addition of the lead acetate the mixture was kept neutralized with ammonium hydroxide. The precipitate was separated in a filter press, the residue washed by slurrying in 45 percent methanol, and again filtered. The residue was discarded and the filtrate retained.

   c. The combined filtrates were treated with 10 percent secondary sodium phosphate to remove lead. For this purpose about six liters of phosphate solution were required. The lead phosphate was filtered off and washed with 45 percent methanol before discarding. The filtrate and washings were combined and evaporated to a quantity of 360 kilograms.

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d. The next operation was carried out at the former Gehe & Company on Leipzigerstrasse 7. The 360 kilogram quantity was further concentrated to 28 kilograms. The temperature was not raised above 45-50°C. during this evaporation in order to avoid destruction of the digitoxin. Strong foaming occurred during this step and was corrected by the use of an antifoam agent made from a silicon compound. This agent was not available in adequate quantities, so octyl alcohol was also employed to reduce foaming.

e. The next step was carried out on a laboratory scale at the Biological Institute of AWD at Stalinstrasse 171. The aqueous concentrate, in 500 cc. lots, was treated with solid sodium chloride and shaken with 350 cc. of chloroform. The aqueous residue was tested for absence of glycoside content and discarded. The chloroform extract was then treated several times with 104 cc. of sodium carbonate and the carbonate solution discarded. The occasional addition of solid sodium chloride during this process prevented the formation of emulsions. The treatment with carbonate solution was continued until the strong red layer first obtained became colorless. The chloroform was then washed with water and the water washings discarded. The chloroform layer was dried over sodium sulfate, filtered, and concentrated under vacuum at 40°C.

f. The concentrated chloroform solution was next treated with petroleum ether. External cooling with ice was applied. This caused the precipitation of crude yellow digitoxin. The precipitate was filtered and washed with petroleum ether. Fifteen grams of crude glycoside, with a glycoside content of 73 percent, was obtained from 50 kilograms of folia Digitalis purpureae.

2. Further attempts to isolate the glycoside were carried out on red and white sea onion. These attempts were still on a laboratory-scale basis in April 1953. Pilot-plant runs had not yet been made. The methods of [redacted] and co-workers, as described in Helvetia Chimica Acta, were followed in this work.

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